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10/590,122

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Naomi Yamakawa

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EXAMINER

STEELE, AMBER D

ART UNIT

PAPER NUMBER

1639

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/590,122	Applicant(s) YAMAKAWA, NAOMI	
	Examiner AMBER D. STEELE	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/11/09, 10/25/09, and 7/7/09.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 1-9, 11-13, 15, and 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10, 14 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 August 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of the Claims

1. Claims 1-11 were originally filed on August 18, 2006.

The preliminary amendment received on August 18, 2006 amended claims 5-7 and added new claims 12-13.

The amendment received on July 7, 2009 amended claim 10 and added new claims 14-20.

Claims 1-20 are currently pending.

Claims 10, 14, and 16 are currently under consideration.

Election/Restrictions

2. Applicant elected, with traverse, Group III (claim 10) in the reply filed on February 12, 2009. Claims 1-9, 11-13, and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

3. Applicant's election without traverse of claim 16 as the species of performing step (2) and DNA fragment mixture in section 3a of claim 10 as the species of DNA fragments prepared in step (1) in the replies filed on October 25, 2009 and December 11, 2009 is acknowledged.

4. Claims 15 and 17-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim.

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Election was made **without** traverse in the replies filed on October 25, 2009 and December 11, 2009.

Priority

5. The present application claims status as a 371 of PCT/JP2005/002490 filed February 17, 2005.

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

7. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. JP 2004-044759 filed February 20, 2004, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. While JP 2004-044759 discloses the species of methylated cytosine, JP 2004-044759 does not provide support for the genus of “modified base” or a “base” as presently claimed. Therefore, the priority date for the present claims is February 17, 2005.

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Withdrawn Objections

7. The objection to the drawings is withdrawn in view of applicants response received July 7, 2009.

8. The objection to the disclosure is withdrawn in view of the amendment received July 7, 2009.

Withdrawn Rejections

9. The rejection of claim 10 under 35 U.S.C. 102(a) as being anticipated by Grigg et al. U.S. 2004/0086944 published May 6, 2004 is withdrawn in view of the claim amendments received on July 7, 2009.

Maintained Rejections

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claim 10 is rejected under 35 U.S.C. 102(e) as being anticipated by Martinssen et al. U.S. Patent 7,186,512 (effective filing date of June 26, 2002).

For present claim 10, Martienssen et al. teach methods for determining the methylation profile of individuals comprising (a) providing a uniformly-sized population of randomly

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cleaved or sheared DNA from a cell, tissue, or organism wherein the DNA comprises a first portion and a second portion and each portion comprises methylated and unmethylated nucleotides, (b) separating the portions into a methylated DNA subportion and an unmethylated DNA subportion via antibodies specific for methylated nucleic acids, and (c) utilizing DNA arrays (please refer to the entire specification particularly columns 1-7, 10-11; Example 4; claims 1, 4, 8-9). Furthermore, Martienssen et al. teach utilization of various restriction enzymes and other methods for fragmenting DNA wherein the restriction enzymes which are not sensitive to modifications and restriction enzymes that produce a ssDNA region (please refer to the entire specification particularly column 9; also see the attached NEB information for methylation sensitivity of various restriction enzymes).

Therefore, the disclosure of Martienssen et al. anticipates the presently claimed method.

Arguments and Response

12. Applicants' arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Martinssen et al. for claim 10 were considered but are not persuasive for the following reasons.

Applicants contend that Martinssen et al. does not teach the DNA fragments of a, b, or c recited in claims 10.

Applicants' arguments are not convincing since the teachings of Martinssen et al. anticipate the method of the instant claims. Martienssen et al. teach utilization of various restriction enzymes and other methods for fragmenting DNA wherein the restriction enzymes which are not sensitive to modifications and restriction enzymes that produce a ssDNA region

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(please refer to the entire specification particularly column 9; also see the attached NEB information for methylation sensitivity of various restriction enzymes).

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph “Written Description” requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Claim 16 is drawn to a method for analyzing a modification in a DNA to be assayed comprising performing at least one antigen-antibody reaction under conditions in which monovalent binding is dissociated and a divalent binding is maintained to separate the mixture into a group consisting of a DNA fragments capable of binding to the antibody by divalent binding and another group consisting of DNA fragments capable of binding to the antibody by monovalent binding. The invention as claimed encompasses all DNA fragments and all antibodies since virtually any antibody can bind any DNA (e.g. specific, nonspecific, etc. under various conditions). The claimed invention states that the DNA fragments are only “capable of”

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binding monovalently or divalently. The claimed invention does not include any structural information regarding the antibodies or DNA fragments except that the DNA fragments contain a base (i.e. redundant since any DNA fragment must contain a base) or a modified base. In addition, the claimed invention does not include any structural information regarding how the DNA fragments bind antibodies monovalently or divalently.

The specification only teaches anti-5-methylcytosine (i.e. one antibody species) and cytosine methylation (i.e. one modified base species) (please refer to the Examples). In addition, the specification only teaches magnetic bead separation of DNA binding to anti-5-methylcytosine on the magnetic beads (please refer to the Examples). Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of anti-5-methylcytosine and cytosine methylation regardless of monovalent or divalent binding as disclosed by the specification, the skilled artisan cannot envision the method of claim 16. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical

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Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

Additionally, Cf. University of Rochester v G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc., No. 03-1304, 2004 WL 260813 (Fed. Cir., Feb. 13, 2004) held that: Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 10, 14, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, since the DNA fragments as claimed must include either "a modified base" or "a base" it is not clear why the restriction enzyme must digest regardless of the presence or absence of a modification (i.e. modified base is not required by the claim). In addition, any restriction enzyme that cleaves and leaves "sticky ends" would produce a ssDNA with an exposed base, therefore, it is not clear how the limitations of b and c are limiting the claimed subject matter (i.e. modified base is not required). Furthermore, does modification include deletions, substitutions, etc.? A nexus between the preamble (i.e. method of

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analyzing a modification in a DNA) and the last method step is missing. Moreover, the claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

17. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. For example, it is not clear how monovalent binding can be dissociated while divalent binding is maintained or why DNA fragments that only associate monovalently with the antibody are deemed to “not react with the antibody” (i.e. monovalent association would be considered a “reaction”). The “capable of” language is also indefinite. In addition, the claim is generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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19. Claims 10 and 14 are rejected under 35 U.S.C. 103(a) as being obvious over Martiensen et al. U.S. Patent 7,186,512 (effective filing date of June 26, 2002) and Makrigiorgos U.S. Patent 7,247,428 filed June 25, 2002 (effective filing date April 23, 2001).

For present claim 10, Martiensen et al. teach methods for determining the methylation profile of individuals comprising (a) providing a uniformly-sized population of randomly cleaved or sheared DNA from a cell, tissue, or organism wherein the DNA comprises a first portion and a second portion and each portion comprises methylated and unmethylated nucleotides, (b) separating the portions into a methylated DNA subportion and an unmethylated DNA subportion via antibodies specific for methylated nucleic acids, and (c) utilizing DNA arrays (please refer to the entire specification particularly columns 1-7, 10-11; Example 4; claims 1, 4, 8-9). Furthermore, Martiensen et al. teach utilization of various restriction enzymes and other methods for fragmenting DNA wherein the restriction enzymes which are not sensitive to modifications and restriction enzymes that produce a ssDNA region (please refer to the entire specification particularly column 9; also see the attached NEB information for methylation sensitivity of various restriction enzymes).

However, Martiensen et al. do not teach nuclease.

For present claim 14, Makrigiorgos teach methods for rapid screening of methylation comprising treating DNA with nuclease to remove single-stranded portions (please refer to the entire specification particularly column 7).

The claims would have been obvious because a particular known technique (i.e. utilizing nuclease) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639